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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,059	11/20/2000	Roy W. Jackson	50124/005001	1634

7590

08/13/2002

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EXAMINER

HUANG, EVELYN MEI

ART UNIT

PAPER NUMBER

1625

DATE MAILED: 08/13/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/582,059

Applicant(s)

JACKSON ET AL.

Examiner

Evelyn Huang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5,7-12,16,18-25,28,29 and 31-33 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,7-12,16,18-25,28,29 and 31-33 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6-5-2002 has been entered.
2. Claims 1-3, 5, 7-12, 14, 16, 18-25, 28, 29, 31-33 are pending. Claims 4, 6, 13; 15, 17 and 30 have been canceled according to the amendment filed on 6-5-2002. Claims 26, 27 have been canceled according to the amendment filed on 8-13-2001.

Claim Rejections - 35 USC § 102

3. The 102(b) rejections over Albertson (4108857), Yokoyama, Atsumi (JP 49072261), Uwaydah, are withdrawn because the amendment has obviated the rejection. The claims have been amended to incorporate the limitation of specific YN moieties and the charged group being amidino or guanidino, thereby setting a demarcation from the prior art compound.
4. The 102(b) rejection over Hogan (WO 94/01102) is withdrawn because the amendment has obviated the rejection. The claims have been amended to incorporate the limitation of specific YN moieties and the charged group being amidino or guanidino, thereby setting a demarcation from the prior art compound.
5. The 102(b) rejection over Jackson is withdrawn because the amendment has obviated the rejection. The claims have been amended to incorporate the limitation of specific YN moieties and the charged group being amidino or guanidino, thereby setting a demarcation from the prior art compound.

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6. The 102 (b) rejection over Maeda is withdrawn for claims 1-5, 23 because the claims have been amended to incorporate the limitation of specific YN moieties, and the charged group being amidino or guanidine, thereby setting demarcation from the prior art compound.

However, the rejection is ***maintained*** for claims 7 and is applicable to new composition claim 31 because the compound with RN 77943-85-2 and the composition thereof, are still encompassed by the instant claims 7, 31 wherein YN is derived from metazocine or pentazocine.

7. The 102 (b) rejection over Atsumi (3950346) is withdrawn for claims 1-5, 18, 23-25 because the claims have been amended to incorporate the limitation of specific YN moieties, and the charged group being amidino or guanidine, thereby setting a demarcation from the prior art compound.

However, the rejection is ***maintained*** for claims 7, and is applicable to new composition claim 31 because the compound of Example 3 (column 5) and the composition thereof, are still encompassed by the instant claims 7, 31 wherein YN is derived from metazocine or pentazocine.

Claim Rejections - 35 USC § 103

8. The 103(a) rejection over Jackson in view of Greene and/or Scheinmann (5977326) is withdrawn upon reconsideration in view of the Declaration submitted by the applicant, and the amendment incorporating the limitation of specific YN moieties and the charged group being amidino or guanidine.

The Declaration demonstrated that Jackson is inoperative prior art. The proviso at the end of claim 1 is to set a demarcation from the compound of Jackson, which has low opiate receptor activity, has been shown to cross the blood brain barrier and has CNS activity (page 23, column 1), thereby teaching away from the instant inventive compound with activity at the peripheral nervous system with little or reduced activity at the CNS system.

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Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 7, 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atsumi (3950346).

Atsumi generically discloses a ketoethylbenzomorphan (column 1, formula I) useful as non-addictive analgesics. A specific example is described on column 5, Example 3.

Atsumi's example has a methyl whereas the instant compound wherein YN is derived from eptazocine has a hydrogen as X. Atsumi, however, teaches that hydrogen and methyl are optional choices (column 1, lines 57-58, definition of R2).

At the time of the invention, one of ordinary skill in the art would be motivated to replace Atsumi's methyl with the alternative hydrogen to arrive at the instant invention with the reasonable expectation of obtaining an additional non-addictive analgesic compound since Atsumi had clearly taught that any species within the disclosed genus would be useful as a non-addictive analgesic.

Claim Rejections - 35 USC § 112(2)

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 7-12, 16, 18-25, 28, 29, 31-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1,

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- In the proviso, is not analgesic activity part of the activity in the CNS? It is recommended the specific CNS side effects, such as sedative or addictive effects, as described on page 3, lines 13-14, be recited in the claims to better define the claim.
- The recitation that 'Y-N is an opioid selected from the group....' is inconsistent with the definition of Y-N in the specification (page 4, lines 14-20 ; page 6, lines 4-11), and claim 7, wherein the recited opioids are precursors of Y-N.
- What is the intended 'spacer'? Definition of 'spacer' should be included to set the metes and bounds of the claim.
- A comma or semicolon is missing between 'or guanidine group' and 'or a pharmaceutically acceptable salt thereof'.

b. Claim 18, it is unclear whether it is a method of use claim or a process of making claim. Since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a method of use without any active, positive steps delimiting how this use is actually practiced. Furthermore, for a method of use claim, the subject and the amount of the compound administered are required but missing in the instant. For a process claim, the product of the reaction steps would be required but is missing.

c. It is unclear how the process of Claims 19-22 would lead to the preparation of a compound of formula II, wherein YN is linked to the amidine or guanidine by an alkylene chain. The steps recited in the claims would only lead to the formation of a compound wherein YN is directly linked to an amidine group as shown in the reaction equations.

d. Claim 20 only recites the steps for making a compound wherein Z is NH or S, the step to make a compound wherein Z is O as recited is missing.

e. Claim 21 only recites the steps for making a compound wherein Z is NH, the step(s) to make a compound wherein Z is O or S as recited is missing.

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- f. Claim 22 recites the reaction of YN-CN and a metallated residue but in the chemical equation, $\text{Na NR}^1\text{R}^2$, $\text{BrMgNR}^1\text{R}^2$, $\text{CH}_3\text{AlClNR}^1\text{R}^2$, which are examples of the metallated residue, are recited. It is unclear whether these examples are (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).
- g. Claim 16, the compounds wherein the amidine group is directly linked to the nitrogen of the opioid moiety has no antecedent basis in the base claim 1 wherein the amidine is linked via a spacer to the nitrogen of the opioid moiety.
- h. In the method Claims 32, 33, the subject to whom the compound is administered is required but is missing in the instant.
- i. Claim 33, line 2, 'composition' is missing after 'pharmaceutical'.
- j. Claim 7, 'R1 and R3 complete a ring', what kind of ring?
- The rejection is applicable to claims dependent on the above claims.

Claim Rejections - 35 USC § 112(1)

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-3, 5, 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation that 'YN is an opioid' has no support in the specification wherein YN is defined as 'an organic group obtained by removal of the R group of the opioid....' on page 4, lines 14-20 of the specification.

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13. Claims 1, 7, 8, 18, 23-25, 32, 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of formula I wherein the spacer has been defined as in claims 2, 3, and the compound of formula II wherein R1 and R3 together with the nitrogen atoms that they are attached form an imidazolyl ring of claim 9 and the does not reasonably provide enablement for the other compounds in the generic claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

For the compounds of formula I wherein the spacer is not described in the specification but embraced by the generic claims, and the compounds of formula II wherein R1 and R3 together form a ring not specifically described in the specification, starting materials and the process for preparation of the inventive compounds is not seen but are required. Sources are particularly pertinent especially when the structures of these spacers or rings are not described. Absent sources, the public is offered mere language, rather than enablement. Ex parte Moersch 104 USPQ 122. In re Howarthe 210.

Duplicate claims

14. Applicant is advised that should claim 24 be found allowable, claim 32 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

15. The subject matter of claim 16 is allowable.

Jackson's compound 23 has disilyl protecting groups, which are absent in the instant. Jackson's compound has low opiate receptor activity, and has been shown to cross the blood brain barrier to elicit CNS activity whereas the instant has analgesic activity with reduced or

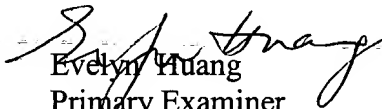
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little CNS side effects. Furthermore, Jackson is inoperative art. The instant compound is therefore unobvious over the compound of Jackson.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is 703-305-7247. The examiner can normally be reached on Tuesday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703-308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Evelyn Huang
Primary Examiner
Art Unit 1625

August 6, 2002